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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,132	11/28/2006	Petronella C. Raemakers-Franken	GRT/4662-216	3817

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EXAMINER	
MEAH, MOHAMMAD Y	

ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
03/05/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/586,132	RAEMAKERS-FRANKEN ET AL.	
	Examiner	Art Unit	
	MD. YOUNUS MEAH	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *15-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5-14* is/are rejected.

7)☒ Claim(s) *4* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/30/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

With preliminary amendment of this application, the applicant, on date 12/10/2007 elected without traverse Group I (claims 1-14) for examination.

Election/Restriction

During preliminary amendment of this application, the applicant, on date 12/10/2007 elected without traverse Group I (claims 1-14), drawn to method of making 6-amino caproic acid using enoate reductase from *clostridium tyrobutyricum* DSM1460 for examination. Groups II-VI (claims 15- 27) of election/restriction-office action of 11/14/07 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Groups.

Priority

This application is a 371 of PCT /EP05/00555 filled 01/17/2005, which claims priority on foreign application of EPO 04075079.6 filled 01/19/2004.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 11/30/2007 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the examiner has considered the IDS statements.

Claim Objections

Claims 2-14 are objected for having non-elected subject matters. Appropriate correction required.

Claim Rejections

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35 U.S.C 112 1st Paragraph

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5-6, 8-14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-3, 5-6, 8-14 are directed to a process of production of 6-amino caproic acid using genus of enoate reductase molecules fro any source or *Acremonium strictum sp*, *Clostridium sp,* etc (referred in claim 2) or *E. coli* species (claim 6). The specification teaches the structure of only a few representative species of such from *clostridium trybutyricum* DSM 1460 and other specific strains as described in claim 4. Moreover, the specification fails to describe any other representative species by any

identifying characteristics or properties other than the functionality of encoding a protein having enoate reductase activity. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

In *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP § 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP § 2163 states that a representative number of species means that the species, which are adequately described, are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Claims 1-3, 5-6, 8-14 are directed to any method of production of 6-amino caproic acid using genus of enoate reductase molecules from a broad genus biological strain. The specification discloses the structure of a few specific enoate reductases (such as *Acremonium strictum* CBS 114157, *Clostridium tyrobutyricum* DS M 1460, *Moorella thermoacetica* DSM 1974, *Ochrobactrum anthropi NCIMB41200*, or *Clostridium kluyveri DSM555*, referred in claim 4) or *E. coli* k12 (claim 7).The specification lacks description of any additional species with structural limitation with function since enoate reductase obtained from these broad spectrum of biological strain comprise many enoate reductases which may or may not produce 6-amino caproic acid from 6-AHEA. Therefore one of skill in the art would not recognize from the disclosure that applicants' were in possession of the claimed invention.

Applicants' are referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Enablement

Claims 1-3, 5-6, 8-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for method of production of 6-amino caproic acid using enoate reductase of *Acremonium strictum* CBS 114157, *Clostridium tyrobutyricum* DS M 1460, *Moorella thermoacetica* DSM1974, etc, does not reasonably provide enablement for method of production of 6-amino caproic acid using any

enoate reductase with any structure or a broad spectrum of enoate reductase from any genus *acetobacterum* sp, from other genus of strains as described in claim 2 or any E coli species (claim 6) . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breath of the claim(s).

Claims 1-3, 5-6, 8-14 are so broad as to encompass any method of production of 6-amino caproic acid using any enoate reductase with any structure or a broad spectrum of enoate reductase from genus *acetobacterum* sp, or from other genus of strains as described in claim 2 or any E coli species (claim 6). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the use of extremely large number enoate reductase broadly encompassed by the claims. In view of the great breaths of claims1-3, 5-6, 8-14, amount of experimentation required to isolate enoate reductase molecules having activity to convert 6-AHEA to 6-amino caproic acid from these enormous number of enoate reductase molecules and , the lack of guidance, working examples, unpredictability of the art in predicting the

function (6-AHEA to 6-amino caproic acid conversion activity) from protein's structure the claimed invention would require undue experimentation. As such the specification fails to teach one of ordinary skill how to use the full scope of the claims.

Since the amino acid sequence of a protein encoded by a polynucleotide determine its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the sequence and respective codons in its polynucleotide, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the encoded proteins' structure relates to its function. However, in this case the disclosure is limited to few enoate reductases (such as enoate reductase of *Acremonium strictum* CBS 114157, *Clostridium tyrobutyricum* DS M 1460, *Moorella thermoacetica* DSM1974).

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompassed any method of production of 6-amino caproic acid using any enoate reductase with any structure or a broad spectrum of enoate reductase from various genus of strains as described in claim 2 or any *E coli* species (claim 6). because the specification does **not** establish: (A) regions of the enoate reductase structure which may be modified without effecting its activity towards 6-AHEA; (B) the general tolerance of enoate reductase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any enoate reductase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any method of production of 6-amino caproic acid using any enoate reductase with any structure or a broad spectrum of enoate reductase from various genus of strains as described in claim 2 or any *E coli* species (claim 6). The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of a CM/PDH gene, having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Conclusion

Prior art (such as Simon et al *Ang. Chem. Int ed* 1983, 539-553, from IDS) teach use of enoate reductase from *Clostridium tyrobutyricum* DSM1460 to reduce R'R''C=CH-COOH to R'R''CH-CH_2-COOH, however there is no anticipation or obvious reasoning to use the said enoate reductase to make 6-amino caproic acid from 6-AHEA.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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